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THYMUS FEEDING IN EXOPHTHALMIC  
GOÏTRE.

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## THYMUS FEEDING IN EXOPHTHALMIC GOÎTRE.

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IN the *British Medical Journal* of February 15th, 1895, I recorded a case of exophthalmic goître of twenty years' duration, in which thymus feeding was followed by restoration of health. The patient first came under observation in May, 1893. Ordinary remedies were tried, but without benefit. After taking raw thymus, obtained from the lamb, in doses of about a quarter of an ounce daily, for three months, the cardinal symptoms disappeared, and the patient was able to work better than he had done for years. The treatment was discontinued in January, 1894. Three months later there was a return of goître, tachycardia, and slight exophthalmos. He then resumed the thymus, taking half an ounce or more of the raw gland three or four times a week. By July, 1894, the eye symptoms and goître had quite disappeared, the pulse was 72, though before treatment it was constantly over 120. He had greatly gained in flesh, felt quite well, and was able to work twelve hours a day as a labourer. The following autumn he found himself unable to take the gland any longer, on account of its nauseating effects. At the end of three months he complained of increasing weakness, and expressed a fear that the old disease was returning. He then again resorted to the thymus, taking it for two months, but this time with no benefit. This was very disappointing, but remembering that the lambing season corresponded with the spring, it occurred to me that the failure of the glands might be due to their having been taken from older sheep than before, so it was resolved to give calf's thymus a trial, as lamb's was not obtainable. On March 22nd, 1895, the patient was worse than I had ever seen him, suffering from intense dyspnœa; the thyroid was large and pulsating, and there was violent throbbing of the carotids. The action of the heart was extremely tumultuous and irregular, pulse over 140. There were marked tremors of the hands, especially the left, and the whole body was much emaciated. The same night he took about half an ounce of calf's thymus, and repeated the dose in the morning. During the following week he improved astonishingly. On March 23rd the patient felt much better, his breathing being much relieved. On March 26th, pulse 126, but the action of the heart not so thumping and irregular as before, and the

dyspnœa was improved. On March 28th the patient felt still better. Exophthalmos decidedly less marked, pulsation in neck scarcely visible, goitre much diminished; tremors less pronounced, pulse 104, heart quiet and more regular, no dyspnœa. My friend, Dr. E. J. W. Carruthers, who had seen the patient just before the calf's thymus was given, on seeing him a week later, shared my surprise at the remarkable improvement which had taken place in so short a time. The next three months he spent mostly in bed, and gastro-intestinal trouble prevented him taking the thymus, except very occasionally. Still, he gradually improved, and by October, 1895, only suffered from debility and emaciation. The improvement continued during the winter, but there was a return of symptoms this summer. He now suffers from occasional palpitation, sense of weakness, and low spirits, and there is some prominence of the eyes. There are, so far, no goitre or tremors, and he is fairly well nourished. The patient is not nearly so well as he was two years ago, but it must be noted that, during the last eighteen months, he has taken much less thymus than before, on account of its nauseating effects, and for nine months has had none at all.

This treatment was also tried in another case of the same disease. A young man, with a history of previous attacks of palpitation, came under observation July 1st, 1895. He said that he began to feel low and weak the preceding Easter, when the warm weather commenced. His friends had been struck by his rapid loss of flesh during the last month, when he had also suffered from vomiting and diarrhœa. During the last six months he had had contractions of the hands, lasting a few seconds, and had lately passed much more water than ordinarily. He had frequently suffered from feelings of heat, particularly in the upper part of the chest, neck, and face, and had sweated profusely, his clothes being often saturated. A couple of years before he had noticed a loss of hair, becoming partially bald, but the hair afterwards grew. When I first saw him the patient had a nervous worried expression, and there was marked exophthalmos, but neither von Graefe's or Stellwag's signs could be elicited. He was very thin. There was considerable swelling of the thyroid—circumference of neck, just about vertebra prominens and upper border of sternum, 16 inches; apex beat visible and diffused in fifth space; loud systolic murmur heard all over cardiac area, but most marked over fourth left costal cartilage, and not conducted towards

angle of scapula. Pulse, after several minutes' rest, was 133; there were marked tremors of the hands, especially the left. The patient was seen again four days later, July 5th. In the meantime he had taken about two ounces of raw cervical thymus, with mint sauce. He said he felt much better; tremors were scarcely perceptible; pulse 124.

On July 7th the patient felt still better, and had been able to play cricket the day before. The thyroid was reduced in size; circumference of neck,  $15\frac{1}{2}$  inches; pulse 133. He stated that he had taken about two ounces of thymus since he saw me last. He remarked that the gland seemed to have a stimulating effect about half an hour after it had been taken. He shortly afterwards went to Scotland for a few days, where he continued taking the thymus, and did so after his return home until the winter. He steadily improved, and has kept well ever since. I saw him last on June 20, 1896. He was then well nourished. Exophthalmos, tremors, palpitation, and pigmentation had all disappeared. Pulse 80. There was still some enlargement of the thyroid; circumference of neck,  $15\frac{1}{2}$  inches. The murmur was still present. The dose taken by these patients was half an ounce to an ounce, two or three times a week, sometimes oftener. The size of the dose tolerated shows how much less potent the thymus is therapeutically than the thyroid, which perhaps is not surprising when we remember that the fully-developed thymus is much larger than the thyroid. The taking of the raw gland is very disagreeable, but probably slightly cooking it would not affect its action; in fact, R. H. Cunningham<sup>1</sup> records two cases, in which giving slightly broiled thymus led to good results. The only pharmaceutical preparation which I have tried is a glycerine extract, specially prepared by Messrs. Woolley, in the proportion of one lobe to the ounce. It was only tried in one case, and though the patient ultimately got quite well, the effect, at first, was not so striking as when the raw gland was given to the other patients. This case was that of a young woman, aged 25, who had found it impossible to take the raw gland. She had been an in-patient seven years before at the Manchester Royal Infirmary, with Graves' disease, and had then recovered her health after a few months' illness. She remained well for five years, but then began again to suffer from palpitation, breathlessness, general weakness, marked loss of flesh, and emotional outbreaks. I saw her on June 16th, 1894. She was very much emaciated; exophthalmos, goitre, and tremors were well



marked. Pulse, after several minutes' rest, 140. Apex beat was outside nipple line in fifth space, and was loud and thumping in character. The patient stayed in bed for six weeks, but during that time refused to take thymus or medicine of any kind, and took very little food, so that her emaciation became extreme, and in no respect was there the slightest improvement. In the early part of August she went to the seaside, and began to take thymus extract in ounce doses daily—equivalent to one lobe of the gland. She steadily improved, and by the end of the month was able to resume her duties as a schoolmistress. Exophthalmos, goitre, and tremors were less marked; the heart was quiet, but still rapid. Pulse 130. The main improvement, however, was a gain of flesh; she also looked and felt better. This might have been due simply to the change of air. On September 8th, patient reported herself feeling much better, notwithstanding having been overworked at school. She had a healthier appearance, and seemed to have gained flesh. Pulsation still visible in the neck. Goitre not much changed. Pulse 116. September 15th, patient said she had had a very heavy week, on account of the illness of the head mistress. She had taken the extract very regularly. Pulse, at first, 132, but after a few minutes' rest, 116. Pulsation in neck not so pronounced as before. Tremors only slight. Goitre about the same. The treatment was continued for another month, but I did not see the patient until January 19th, 1896. She then told me that the giving up of the extract made no difference to her, but she went on improving just the same as before. She looked quite well and stout. Pulse 84. No tremors or exophthalmos. There was still some fulness in the neck, scarcely amounting to a goitre. She was shortly afterwards married, and left the neighbourhood, and I have not seen her since.

Since my communication on this subject appeared in the *Journal*, others have published confirmatory results.

Mikuliez<sup>2</sup> found that nine out of ten cases of ordinary goitre were improved by thymus, and in a case of Graves' disease he noted improvement in palpitation, dyspnoea, and attack of threatened suffocation. The exophthalmos and tachycardia were likewise diminished, but goitre and tremors remained the same. The dose given varied, roughly speaking, from half an ounce to an ounce of the raw gland.

R. H. Cunningham<sup>1</sup> has treated several cases at the Vanderbilt Clinic and in private practice, with results which he describes as

"surprising, gratifying, and very suggestive." Three of his cases are described in full in the *Medical Record* of June 15, 1895.

Robert T. Edes<sup>3</sup> reports a case treated in the Adams Nervine Asylum for nine months with no favourable result. "Thymusine" was then tried, and in three weeks the patient was discharged "relieved." The improvement continued as long as the treatment was followed, but after stopping it "the patient began to feel not so well." On resuming the treatment the patient again improved, and was able to return to her work at a busy time.

Prof. S. Solis Cohen, Philadelphia, has tried thymus in several cases, followed by "great improvement."<sup>4</sup> One case which improved under thymus was made worse by thyroid.<sup>5</sup>

Norman J. McKie<sup>6</sup> has also reported favourably of the treatment in the *Journal*.

+ Maude,<sup>21</sup> whose previous writings on Graves's disease enhance the value of his testimony, has tried the thymus treatment in four cases of this disease with most gratifying results. All were benefited. In one case of an extremely aggravated form, which had been under observation over eight years, no drug, not even belladonna in large doses, had ever produced any effect. Under thymus tabloids (45grs. per diem) the patient rapidly improved, but always relapsed when they were discontinued. I can quite endorse Dr. Maude's observation that the tremors are particularly relieved by this treatment. This fact so impressed me a year ago that I tried fresh thymus in a case of paralysis agitans, with the result that the tremors were unmistakably benefited, and the mental state and the muscular condition were greatly improved. The patient felt so much better, and his spirits were so buoyant last Christmas that he astonished his family by "letting in the New Year" himself, a practice which he had always observed before his illness, but had been obliged to omit for years.

C. Todd, in *Journal* of July 25th, 1896, shows clearly how a case of this disease, which had been treated in Shoreditch Infirmary for four months without benefit, was immensely improved at once by thymus tabloids. An irregular pulse became quite regular, as shown by tracings, in three days, and pulse-rate was reduced from 156 to 72 in three weeks. Discontinuance of the treatment caused the pulse to become irregular again, but on resuming the thymus, the irregularity ceased.

Watson-Williams<sup>7</sup> has recorded a case in which thymus feeding apparently aggravated the tachycardia and pyrexia, but improved the general nutrition, the body weight being increased by four pounds in a week. It is rather doubtful whether the aggravation of symptoms was due to the treatment, as the pulse rate was much higher when only 30 grains per diem was being taken, than when half an ounce was the daily dose. The temperature also reached a higher point a week after the thymus was stopped, than it had done while the treatment was being carried out.

The relief obtained in these cases must have been more than a coincidence, as in one of my cases and in several recorded by others, discontinuance of the gland was followed by relapse, but on resuming it the patients again improved.

The thymus, spleen, and other lymphoid structures have been often found hypertrophied in this disease. Hypertrophy or "revival" of the thymus has been observed by Möbius, Marie, Johnston, Hale White, Mossler, Spencer, and several others.<sup>1</sup> Joffroy<sup>13</sup> asserts that the latter condition occurs almost exclusively in exophthalmic goitre. There are grounds for believing that the hypertrophy of the thymus and spleen is compensatory in character, their internal secretions exerting an antidotal influence in a disease most probably of toxic origin. This is suggested by the fact that "the introduction of bacterial poisons into the blood causes increased activity of lymphoid structures, as is shown by the leucoeytosis"<sup>22</sup> which results; and as leucocytosis may serve an antitoxic purpose, it seems probable that the hypertrophy of the thymus and spleen in Graves' disease is the result of a physiological attempt to supply an antidote. Moreover, Poehl<sup>9</sup> has shown that a thymus infusion possesses antitoxic qualities, and Montouri<sup>10</sup> found that splenectomy is followed by diminished bactericidal powers of the blood. Splenic extract has actually been found beneficial in Graves' disease by Professor Wood, of Philadelphia.<sup>11</sup> One case was apparently cured, and two benefited. He was led to try the treatment in consequence of having observed a case of Graves' disease undergo spontaneous cure when complicated with abscess of spleen.<sup>12</sup> Further confirmation of this theory is afforded by the fact that cases of Graves' disease are often improved by pregnancy. Charcot was so impressed with this coincidence that he actually prescribed pregnancy as a remedy



in a case which he saw in consultation with Trousseau.<sup>13</sup> Sir Walter Foster<sup>14</sup> has stated that the worst case of this disease he ever saw was cured by pregnancy. This improvement is all the more remarkable on account of the increased tendency to goitre during pregnancy,<sup>13</sup> and of the fact that functional activity of the sexual organs is associated with increased activity of the thyroid.<sup>15</sup> The fact that the spleen enlarges during pregnancy, and physiological leucocytosis exists,<sup>16</sup> suggests that the improvement may be due to increased lymphoid activity. This suggestion is not disproved by the observation of Joffroy, that Graves' disease may be aggravated during pregnancy,<sup>13</sup> as the increased thyroidal activity may not be sufficiently neutralised. It is also significant that this disease is almost unknown until after the period when the thymus normally disappears, which is remarkable when we remember that the thyroid is more active in early life than it is later on,<sup>15</sup> and, therefore, one would expect a greater tendency to hyperthyroidisation. In view of the fact that exophthalmic goitre is probably due to excessive activity on the part of the thyroid gland, it is of interest and importance to find evidence of antagonism between it and other ductless glands. Dr. George Oliver<sup>17</sup> has lately shown that the thyroid and adrenals have an opposite action to one another upon the circulation, and has found that the curve of blood pressure produced by splenic extract differs from that of thyroid. The action of the thymus has not yet, I believe, been investigated, but in some respects, at least, it appears to be opposed to the thyroid. The administration of thyroid extract is often followed by loss of body-weight. On the other hand, the fact that the thymus is normally only present during infancy, when for the purpose of growth the necessity of minimising waste is obvious, and that it is persistent in hibernating animals, undergoing enlargement at the approach of each hibernation, suggests strongly that this gland has an inhibitory influence over waste. This inference is supported by Demme's case, reported by Jacobi,<sup>18</sup> of a child which underwent rapid emaciation, dying on the forty-second day. Necropsy revealed no change in any other organ except the thymus, whose tissue was dense, and contained three tubercles. Further confirmation is afforded by the experience of Friedleben,<sup>19</sup> who saw a dog die of exhaustion, in spite of a voracious appetite, after extirpation of the thymus and spleen. In all of my cases a gain of flesh accompanied the disappearance of symptoms.

Some facts also suggest the possibility of an antagonism between the thymus and thyroid in their relationship to the nervous system. The thyroïdal secretion directly or indirectly has a stimulating influence over the cerebral functions, as is shown by their undeveloped condition in cretinism and their degeneration in myxœdema and after thyroidectomy, and also by the effects following the administration of thyroid extract in cases of cretinism. There are reasons, too, for believing as pointed out by Freund and Horsley,<sup>15</sup> that the activity of the thyroid gland is increased when active changes are taking place in the sexual system. On the other hand, during hibernation, when the thymus attains its greatest size,<sup>20</sup> the cerebral and sexual functions are suspended, and in infancy are undeveloped, but undergo rapid development at puberty, when the thymus finally disappears. These facts suggest a functional relationship between the different ductless glands, and lead one to think that disease may result from disturbance in the balance of their internal secretions, which might be remedied by suitable animal extracts.

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